

WE CLAIM:

SUB
8 CD

1. A method of increasing the expression of an immune response recognition molecule in a mammalian cell by introducing a double-stranded polynucleotide into the cell comprising, activating expression of a gene or gene product involved in antigen presentation, growth, and function of the cell, and increasing the ability of a cell to present antigen to an immune cell.

2. The method of claim 1 wherein the molecule is derived from the major histocompatibility complex (MHC).

3. The method of claim 1 wherein the double-stranded polynucleotide is greater than 25 base pairs in length.

10
SUB
DZ

4. The method of claim 1 wherein the double-stranded polynucleotide is derived from a source selected from the group consisting of a bacterium, protozoan, virus, and mammalian cell.

5. The method of claim 1 wherein the double-stranded polynucleotide is chemically synthesized without using an enzyme.

15
SUB
DZ

6. The method of claim 1 wherein the double-stranded polynucleotide is located in the cytoplasm of the cell.

7. The method of claim 6 wherein the double-stranded polynucleotide is DNA leaking from the cell's nucleus or mitochondria after injuring the cell with an exogenous or environmental stimulus.

20

8. The method of claim 1 wherein the double-stranded polynucleotide is introduced by transfection, microinjection, or direct injection using a needle or gene gun.

9. The method of claim 1 wherein the double-stranded polynucleotide is introduced by viral infection of the cell.

SUB
DZ
CON'T.

10. The method of claim 1 wherein introduction of the double-stranded polynucleotide into the cell occurs by phagocytosis of a bacterium, virus, or cell.

11. The method of claim 1 wherein introduction of the double-stranded polynucleotide into the cell occurs by oncogene transformation.

12. The method of claim 1 wherein the cell expresses an autoantigen.

13. The method of claim 1 wherein the cell is selected from the group consisting of non-immune cell, immune cell, antigen presenting cell, and thyroid cell.

14. The method of claim 13 wherein the thyroid cell is the FRTL-5 thyrocyte.

15. The method of claim 2 wherein a MHC Class I expression increases greater than a MHC Class II expression as a function of time after introduction of concentration of the double-stranded polynucleotide.

16. The method of claim 2 wherein expression of the MHC molecule is measured by determining abundance of MHC protein, MHC transcripts, or MHC gene transcription.

17. The method of claim 1 wherein expression of the MHC molecule is accompanied by increased expression of an about 90 kilodalton tumor-associated immunostimulator.

18. The method of claim 17 wherein the 90 kilodalton tumor-associated immunostimulator is an intermediate in the expression of the MHC class I molecule.

19. The method of claim 1 wherein the gene or gene product is selected from the group consisting of TAP-1, TAP-2, a proteosome subunit, HLA-DM, invariant chain, CIITA, RFX5, B7 costimulatory molecule, PKR, IFN-beta, MAP Kinase, NF- κ B, JAK, and a STAT.

20. The method of claim 1 wherein expression of the gene or gene product is activated through a cellular signal selected from the group consisting of phosphorylation, ADP ribosylation, and proteolytic cleavage.

21. The method of claim 1 wherein the cell can induce an autoimmune response when injected into its host organism.

22. The method of claim 1 wherein the cell recruits and activates T cells when injected into

SUB
D5
CON't.
July 91

its host organism.

23. The method of claim 1 wherein the cell produces at least one soluble mediator of immunity.

24. The method of claim 2 wherein increasing expression of the MHC molecule by double-stranded polynucleotide is additive to and independent of an interferon-mediated increase in expression of the MHC molecule.

SUB
D6

25. The method of claim 1 wherein the double-stranded polynucleotide is RNA that increases β -interferon production by the cell.

26. The method of claim 1 wherein introduction of the double-stranded polynucleotide increases immunogenicity of the cell in a host organism and, further comprising, immunizing the host organism with the cell.

27. The method of claim 25 wherein the cell is a tumor cell and the immunized host organism has an increased ability to recognize and kill the tumor cell.

28. A method for increasing presentation of antigen by a cell derived from a host organism comprising:

- a) introducing a double-stranded polynucleotide into the mammalian cell;
- b) increasing the mammalian cell's ability to present antigen and forming an activated antigen presenting cell (APC); and
- c) measuring increases in expression of at least one major histocompatibility complex (MHC) molecule in or on the activated APC, and of at least one non-MHC molecule involved in antigen presentation in or on the activated APC.

29. ~~The method of claim 28 wherein the cell is a mammalian cell.~~

30. The method of claim 28 wherein neither strand of the polynucleotide encodes an MHC molecule or a non-MHC molecule involved in antigen presentation.

SUB
D7
CONT.

31. The method of claim ~~28~~ wherein increases in expression of the MHC molecule and the non-MHC molecule involved in antigen presentation are measured by determining that the mammalian cell's ability to present antigen is increased.

5
SUB
EP

32. The method of claim 28 wherein an increase in expression of both MHC Class I and Class II molecules in or on the activated APC is measured.

33. The method of claim 28 wherein the double-stranded polynucleotide comes from the mammalian cell's nucleus or mitochondria.

SUB
D8
CONT.

34. ~~The immunization method according to claim 27 and further comprising introduction of the activated APC into the host animal.~~

35. The method of claim 34 wherein immunization causes an autoimmune reaction in the host animal.

36. A screening method for a drug to regulate antigen presentation comprising:

- a) introducing a double-stranded polynucleotide into a mammalian cell;
- b) measuring expression in or on the mammalian cell of at least one molecule selected from the group consisting of major histocompatibility complex (MHC) molecule and non-MHC molecule involved in antigen presentation;
- c) mixing the mammalian cell with or without a candidate drug; and
- d) measuring an increase or decrease in the mammalian cell's ability to present antigen after introduction of the double-stranded polynucleotide when incubations with or without the candidate drug are compared.

20

37. The method of claim 36 wherein the introduction of a double-stranded polynucleotide is coincident with or after the incubation with or without a candidate drug.

38. A method for drug screening comprising:

a) introducing double-stranded polynucleotide into a mammalian cell,

- b) treating the cell with the drug before, coincident with or after introducing double-stranded polynucleotide, and
- c) measuring expression of major histocompatibility complex (MHC) molecules and about a 90 kilodalton tumor-associated immunostimulator gene expression about 12 or more hours after treating the cell with the drug in step (b) is performed.

39. The method of claim 38 wherein the drug is MMI, an MMI derivative, a thione or a thione derivative.

40. A pharmaceutical composition wherein the composition includes a drug capable of preventing tissue damage caused by an autoimmune reaction, preventing atherosclerotic plaque development, treating autoimmune disease, treating an infection, treating transplantation rejection, or treating tumor cells, comprising an effective amounts of Methimazole, methimazole derivatives, or tautomeric cyclic thiones.

41. A DNA molecule comprising at least one of SEQ ID NOS: 1-16.

42. The method of claim 1 wherein the cell recruits and activates other T or B cells to enhance the immune response.

43. The method of claim 2 wherein increasing expression of the MHC molecule by double-stranded polynucleotide is additive to or independent of an interferon-mediated increase in expression of the MHC molecule.

44. The method of claim 13 wherein the double-stranded polynucleotide is RNA that increases β -interferon production by the immune or antigen presenting cell.

45. The method of claim 13 wherein the immune or antigen presenting cell is a tumor cell and the host organism has an increased ability to recognize and kill the tumor cell.

46. An antigen presenting cell (APC) capable of increasing presentation of an antigen by a mammalian cell derived from a host organism comprising:

- ~~sub
B2
cost.~~ →
- a) introducing a double-stranded polynucleotide into the mammalian cell;
 - b) increasing the mammalian cell's ability to present antigen and forming an activated antigen presenting cell (APC); and
 - c) measuring increases in expression of at least one major histocompatibility complex (MHC) molecule in or on the activated APC, and of at least one non-MHC molecule involved in antigen presentation in or on the activated APC.
- 5

add Af
add c7

ADD
D14 →